

AMENDMENT TO THE CLAIMSCLAIM AMENDMENTS UNDER THE PROVISION OF 37 CFR § 1.121(c)(1)(i)

1. (Currently Amended) A method of treating a TNF α -related disorder in a subject, wherein the TNF α -related disorder is ~~selected from the group consisting of a spondyloarthropathy, a pulmonary disorder, a coronary disorder, a metabolic disorder, anemia, pain, a hepatic disorder, a skin disorder, a nail disorder, or vasculitis,~~ comprising administering to the subject a therapeutically effective amount of a neutralizing, high affinity human TNF α antibody, such that said TNF α -related disorder is treated.
2. (Currently Amended) A method of treating a TNF α -related disorder in a subject, wherein the TNF α -related disorder is ~~selected from the group consisting of Behcet's disease, ankylosing spondylitis, asthma, chronic obstructive pulmonary disease (COPD), idiopathic pulmonary fibrosis (IPF), restenosis, diabetes, anemia, pain, a Crohn's disease related disorder, juvenile rheumatoid arthritis (JRA), a hepatitis C virus infection, psoriasis, psoriatic arthritis, and chronic plaque psoriasis,~~ comprising administering to the subject a therapeutically effective amount of a neutralizing, high affinity human TNF α antibody, such that said TNF α -related disorder is treated such that said TNF α -related disorder is treated.
3. (Canceled)
4. (Currently Amended) The method of any one of claims 1, or 2, ~~or 3~~, wherein the antibody is an isolated human antibody, or an antigen-binding portion thereof, that dissociates from human TNF α with a K_d of 1×10^{-8} M or less and a K_{off} rate constant of $1 \times 10^{-3} \text{ s}^{-1}$ or less, both determined by surface plasmon resonance, and neutralizes human TNF α cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1×10^{-7} M or less.
5. (Currently Amended) The method of any one of claims 1, or 2, ~~or 3~~, wherein the antibody is an isolated human antibody, or an antigen-binding portion thereof with the following characteristics:
 - a) dissociates from human TNF α with a K_{off} rate constant of $1 \times 10^{-3} \text{ s}^{-1}$ or less, as determined by surface plasmon resonance;

b) has a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8 and/or 9;

c) has a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10 or 11 or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12.

6. (Currently Amended) The method of any one of claims 1, or 2, ~~or 3~~, wherein the antibody is an isolated human antibody, or an antigen-binding portion thereof, with a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO:1 and a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2.

7. (Currently Amended) The method of any one of claims 1, or 2, ~~or 3~~, wherein the antibody is D2E7.

8. (Currently Amended) A method of treating a subject suffering from a TNF α -related disorder, wherein the TNF α -related disorder is ~~selected from the group consisting of Behcet's disease, ankylosing spondylitis, asthma, chronic obstructive pulmonary disease (COPD), idiopathic pulmonary fibrosis (IPF), restenosis, diabetes, anemia, pain, a Crohn's disease related disorder, juvenile rheumatoid arthritis (JRA), a hepatitis C virus infection, psoriasis, psoriatic arthritis, and chronic plaque psoriasis,~~ comprising administering a therapeutically effective amount of a TNF α antibody, or an antigen-binding fragment thereof, to the subject, wherein the antibody dissociates from human TNF α with a K_d of 1×10^{-8} M or less and a K_{off} rate constant of $1 \times 10^{-3} \text{ s}^{-1}$ or less, both determined by surface plasmon resonance, and neutralizes human TNF α cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1×10^{-7} M or less, such that said TNF α -related disorder is treated.

9. (Currently Amended) A method of treating a subject suffering from a TNF α -related disorder, wherein the TNF α -related disorder is ~~selected from the group consisting of Behcet's disease, ankylosing spondylitis, asthma, chronic obstructive pulmonary disease (COPD), idiopathic pulmonary fibrosis (IPF), restenosis, diabetes, anemia, pain, a Crohn's disease related disorder, juvenile rheumatoid arthritis (JRA), a hepatitis C virus infection, psoriasis, psoriatic arthritis, and chronic plaque psoriasis,~~ comprising

administering a therapeutically effective amount a TNF α antibody, or an antigen-binding fragment thereof, with the following characteristics:

- a) dissociates from human TNF α with a K_{off} rate constant of $1 \times 10^{-3} \text{ s}^{-1}$ or less, as determined by surface plasmon resonance;
- b) has a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8 and/or 9;
- c) has a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10 or 11 or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12, such that said TNF α -related disorder is treated.

10. (Currently Amended) A method of treating a subject suffering from a TNF α -related disorder, wherein the TNF α -related related disorder is selected from the group consisting of Behcet's disease, ankylosing spondylitis, asthma, chronic obstructive pulmonary disease (COPD), idiopathic pulmonary fibrosis (IPF), restenosis, diabetes, anemia, pain, a Crohn's disease related disorder, juvenile rheumatoid arthritis (JRA), a hepatitis C virus infection, psoriasis, psoriatic arthritis, and chronic plaque psoriasis, comprising administering a therapeutically effective amount a TNF α antibody, or an antigen-binding fragment thereof, with a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 1 and a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2, such that said TNF α -related disorder is treated.

11. (Currently Amended) The method of any one of claims 8, 9, or 10, wherein the TNF α antibody, ~~or antigen-binding fragment thereof,~~ is D2E7.

12. The method of any one of claims 8, 9, or 10, wherein the TNF α antibody is administered with at least one additional therapeutic agent.

13. (Currently Amended) A method of treating a subject suffering from a TNF α -related disorder, wherein the TNF α -related related disorder is selected from the group consisting of Behcet's disease, ankylosing spondylitis, asthma, chronic obstructive pulmonary disease (COPD), idiopathic pulmonary fibrosis (IPF), restenosis, diabetes, anemia, pain, a Crohn's disease related disorder, juvenile rheumatoid

~~arthritis (JRA), a hepatitis C virus infection, psoriasis, psoriatic arthritis, and chronic plaque psoriasis,~~
comprising administering a therapeutically effective amount of D2E7, of an antigen binding fragment thereof, such that said TNF α -related disorder is treated.

14. The method of claim 13, wherein D2E7 is administered with at least one additional therapeutic agent.

15-17. (Canceled)